

CLAIMS

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- 5 1. The use of an inhibitor of the interaction of glutamate with the AMPA receptor complex and of the interaction of glutamate with the kainate receptor complex in the manufacture of a medicament for treating a demyelinating disorder.
2. The use of an inhibitor of the interaction of glutamate with the AMPA receptor complex in the manufacture of a medicament for treating a demyelinating disorder.
- 10 3. The use of an inhibitor of the interaction of glutamate with the kainate receptor complex in the manufacture of a medicament for treating a demyelinating disorder.
- 15 4. The use according to any preceding claim, wherein the demyelinating disorder is acute disseminated encephalomyelitis, acute demyelinating polyneuropathy (Guillain Barre syndrome), chronic inflammatory demyelinating polyneuropathy, multiple sclerosis, Marchifava-Bignami disease, central pontine myelinolysis, Devic syndrome, Balo disease, HIV- or HTLV-myelopathy, progressive multifocal leucoencephalopathy, or a secondary demyelinating disorder.
- 20 5. The use according to any of claims 1 to 3, wherein the secondary demyelinating disorder is CNS lupus erythematoses, polyarteritis nodosa, Sjögren syndrome, sarcoidosis or isolated cerebral vasculitis.
- 25 6. The use according to any of claims 1 to 5, wherein the inhibitor is an antagonist of the binding of glutamate to the AMPA receptor.
7. The use according to any of claims 1 to 5, wherein the inhibitor is an antagonist of the binding of glutamate to the kainate receptor.

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8. The use according to any preceding claim, wherein the inhibitor is an L-glutamate derivative, an α -amino-3-hydroxy-5-methyl-4-isoxazolepropionate derivative, arylthioxaline (42), acid amide (59), hydrazone (48), quinoline (51), quinolinone (70,78), quinoxaline (8,9,13,14,15,17,20,47,50,52,53,54,55,56),
 5 quinoxalinedione (7,11,23,43,57,58,60,61,74,77,81), triazoloquinoxalinedione (3,4,5), pyrrolylquinoxalindione (6), quinazolinone (22), quinazolinedione (35), quinoxalinone (29), phenylpyridazinoindoleione (41), indenopyrazinone (24,32,63,65,66,67,68), imidazoloquinoxalinone (12), indolo-pyrazinone (64), imidazo-pyrazinone (31,33,34,37,44,62), triazolo-pyrazinone (30), benzothiadiazine (16,36), 4-
 10 hydroxypyrrolone, pyrrolo-pyridazinone (40), phthalazine (25), quinolone (18,19), amino-alkanoic acid (1), isatine (72), phenyl-azolophthalazine, amino- or desamino-2,3-benzodiazepine (10,26,27,28,38,49,79), 2,3-benzodiazepin-4-one (21), imidazobenzodiazepine (71), β -carboline-3-carboxylic acid, alkoxy-phenyl-benzodiazepine, isoquinolinyl-carboxylic acid derivatives (75), acetyl-aminophenyl-
 15 dihydro-methyl-dioxolo-benzodiazepine, pyrimidinone (46), oxadiazol (80), isatinoxime, decahydroisoquinoline (69,73,76), piperazine derivative (2), tetramic acid derivatives (39), or a sulphamate. (The reference numbers used above correspond with the numbers used in the list of antagonists provided in the description.)
- 20 9. The use according to any of claims 1 to 7, wherein the inhibitor is L-glutamic acid diethylester, 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline (NBQX), 6,7-dinitro-quinoxaline-2,3-dione (DNQX), 6-nitro-7-cyano-quinoxaline-2,3-dione (CNQX), 6-(1-imidazolyl)-7-nitro-quinoxaline-2,3(1H,4H)-dione (YM90K), (3RS,4aRS,6RS,8aRS)-6-(2-(1H-tetrazole-5-yl)ethyl)-decahydroiso-quinoline-3-
 25 carboxylic acid (LY293558), 9-methyl-amino-6-nitro-hexahydro-benzo(F)quinoxalinedione (PNQX), 8-methyl-5-(4-(N,N-dimethylsulphamoyl)phenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2h]-isoquinoline-2,3-dione-3-O-(3-hydroxybutyric acid-2-yl)oxime (NS 1209), 6,7-dichloro-2-(1H)-quinolinone-3-phosphonate (S 17625-2), and [1,2,3,4-tetrahydro-7-morpholinyl-2,3-dioxo-6-(trifluoromethyl)quinoxalin-1-
 30 yl]methyl-phosphonate (ZK200775), 1-(4-aminophenyl)-4-methyl-7,8-methylene-

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5 dioxo-5H-2,3-benzodiazepine (GYKI52466), (-)-1-(4-aminophenyl)-4-methyl-7,8-methylenedioxy-4,5-dihydro-3-methylcarbamoyl-2,3-benzodiazepine (GYKI53773), topiramate, 3-(2-chlorophenyl)-2-[2-[6-[(diethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-4(3H)-quinazolinone (CP465022) and 5-(2-[N,N-dimethylamino]oxyphenyl)-3-phenyl-1,2,4-oxadiazol (BIIR561).

10. The use according to any of claims 1 to 5, wherein the inhibitor is an AMPA receptor channel blocker.

10 11. The use according to any of claims 1 to 5, wherein the inhibitor is a kainate receptor channel blocker.

12. The use according to claim 10, wherein the AMPA receptor channel blocker is fluorowillardiine or Joro spider toxin.

15 13. The use according to claim 11, wherein the kainate receptor channel blocker is fluorowillardiine or Joro spider toxin.

20 14. The use according to any preceding claim wherein the inhibitor is combined with one or more of: an immunosuppressive agent (e.g. corticotrophin, a glucocorticoid, cyclophosphamide, cyclosporine, azothioprine or mitozantrone), an interferon (IFN; IFN-beta-1a e.g. Rebif and Avonex; IFN-beta-1b e.g. Betaseron and Betaferon; IFN-alpha-2a e.g. Alphaferone; IFN-alpha-2b e.g. Viraferon), a phosphodiesterase type IV inhibitor, a humanised monoclonal antibody against a
25 leukocyte adhesion molecule (e.g. Antegran), a synthetic polypeptide (e.g. glatiramer acetate, copolymer-1), a tissue matrix metalloproteinase (MMP) inhibitor (e.g. hydroxamic acid-based inhibitors of MMPs), or a tumour necrosis factor (TNF) inhibitor (e.g. Thalidomide or TNF-receptor immunoglobulin fusion protein).

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15. A pharmaceutical composition comprising an inhibitor as described in any of claims 1 to 14 and a pharmaceutically acceptable carrier.
- 5 16. A combined preparation of an inhibitor as described in any claims 1 to 14 and one or more of: an immunosuppressive agent (e.g. corticotrophin, a glucocorticoid, cyclophosphamide, cyclosporine, azothioprine or mitozantrone), an interferon (IFN; IFN-beta-1a e.g. Rebif and Avonex; IFN-beta-1b e.g. Betaseron and Betaferon; IFN-alpha-2a e.g. Alphaferone; IFN-alpha-2b e.g. Viraferon), a phosphodiesterase type IV inhibitor, a humanised monoclonal antibody against a leukocyte adhesion molecule
- 10 (e.g. Antegran), a synthetic polypeptide (e.g. glatiramer acetate, copolymer-1) a tissue matrix metalloproteinase (MMP) inhibitor (e.g. hydroxamic acid-based inhibitors of MMPs) or a tumour necrosis factor (TNF) inhibitor (e.g. Thalidomide or TNF-receptor immunoglobulin fusion protein)
- 15 for simultaneous, separate or sequential use in the treatment of a demyelinating disorder.
17. The invention substantially as hereinbefore described.

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